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CONTRIBUTIONS TO OUR KNOWLEDGE OF THE USE OF ANIMAL EXTRACTS.

BY J. G. SHOEMAKER, M.D.

Surgeon to the Phoenixville Hospital

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H. C. WOOD, M.D.

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PART I.

Addison's Disease. CASE I.—Extract of Suprarenal Capsules used.

By J. G. SHOEMAKER, M.D.,
Surgeon to the Phoenixville Hospital.

THE following case of Addison's disease is of especial interest on account of the apparent results caused by the hypodermic use of a glycerin extract of the suprarenal capsules. Careful examination of the family history of the patient, a woman of 30 years, failed to detect any neurotic or other hereditary taint in the stock.

May 30, 1892, Mrs. E. was suddenly taken ill with vomiting, without apparent cause. At that time her weight was 140 pounds, and she considered herself in good health. The vomiting occurred almost daily, but during the summer she gained in weight, so that in September she weighed 186 pounds. During 1893 the vomiting continued, and she steadily lost weight, but was nevertheless able to attend to her family duties, and first reported to me for medical treatment in December, 1893. At that time she was in a condition of profound exhaustion, with malaise, inability to walk 300 yards without rest, and vomiting almost constant. There was some headache, with frequent attacks of dizziness, also of intense rectal pain. Her prostration became so pronounced that she was confined to bed, being unable to raise her head from the pillow. Fainting spells were frequent, at times lasting an hour or two, and vertigo was marked and accompanied by the "taste of blood" in her mouth, as she expressed it. Her pulse

was weak and thready, but regular and 80 per minute. Excepting the rectal pain before mentioned, which lasted about one week, she has never during her illness suffered any pain. There have been no hysterical manifestations whatever, and no history of any. She has always been irregular in her diet. The vomiting is peculiar. There is never any nausea. There is simply one regurgitant movement and the stomach is evacuated at once. At times there is considerable eructation of gas, but never any acid or bilious vomit. The appetite is not impaired. The odor of vinegar or anything sour will bring on attacks of intestinal colic, which are severe, yet there is a decided dislike for sweets.

The face is of a dark copper color, with very dark rings around the eyes. At times it takes on greenish hues. The lips are pale, the gums are discolored in spots, and about the line of the teeth in the lower jaw there is a dark line resembling the line in lead-poisoning. The lower teeth are fairly well preserved. She wears a plate in the upper jaw. The tongue is slate-colored, more or less coated, never pink. The inside of the cheeks is rather dark. The roof of the mouth is of normal color. The skin on the neck is dark, fading to a lighter color as the breasts are reached. There are dark rings around the nipples. The skin on the back is natural in color; that on the hands and the rest of the body is moderately light. The base of the nails is markedly white, and the finger-tips are pale. The bowels are usually constipated. There is never any diarrhea.

Physical examination of the abdomen and thorax proves negative, except that the heart-sounds are weak. Uterus and appendages normal, except a small stellate laceration of the cervix. The hair is black, dull, dry, and curly, and falling out considerably during the past year; previously it was glossy and abundant. The thyroid gland is normal, and there is no glandular enlargement anywhere. Examination of the urine proved negative.

Dr. James Thorington, of Philadelphia, who first suggested the diagnosis of Addison's disease, states that the optic nerve and fields are normal for both form and color; that the ophthalmoscope shows in each eye: media clear, nerve large, oval, axis horizontal, vessels normal, and no gross changes noted; and that there is myopic astigmatism.

Examination of the blood, made in March, 1894, by Dr. Geo. B. Wood, showed the red blood-corpuscles a little below normal, 4,400,000; the white blood-corpuscles slightly above 205-12; hemoglobin, 54 per cent. Of the protoplasmic corpuscular bodies there were:

Lymphocytes	10 per cent.
Large mononuclear	10 "
Transitional	2 "
Multinuclear	76 "
Eosinophiles	2 "

In February, 1894, the symptoms became worse and worse; there was also developed a profuse menorrhagia. The patient was confined absolutely to bed, fainting being produced simply by raising her into a semi-sitting position. In spite of careful treatment the condition became more and more serious until April 1, 1894, when she was seen by Dr. H. C. Wood, who suggested hypodermic injections of the glycerite of the suprarenal capsule of the beef. He then had a veterinary surgeon procure us the capsules from the freshly-killed beef, and had a liquid extract in glycerin prepared by the vacuum process (after the Brown-Séquard method), fifteen minimis representing ten grains of the capsule. Before the injections were started she was taking nourishment freely, but vomited continuously the liquid diet. The quantity of diet did not influence the vomiting, a tablespoonful of milk being rejected as surely as a glassful.

The first injection was given April 4, at which time her weight had fallen to eighty-nine pounds. The temperature varied from half a degree subnormal to a degree above the norm.

April 8. Temperature, morning, $98\frac{2}{5}$ ° F.; evening, $97\frac{4}{5}$ ° F.; 12 minimis of the glycerin extract injected. Soreness of both arms at points of injection, with threatened abscess on left arm. Headache and sense of fulness and brow pains were noted.

April 9. Injection of 15 minimis. Headache continues. Pulse 66. Administered quarter-grain doses of the hydrochlorate of hydrastinine every four hours. Still vomits. Fainting spells on rising in bed.

April 13. Injected 15 minimis each morning, alternating between right and left arm on account of the irritation produced by the injections. Morning temperature, $99\frac{2}{5}$ ° F.; evening temperature, 99° F. Has slight headache, but says she feels better. Weight 101 pounds. The patient was weighed once a week on suspended scales in her night-robe. All of the succeeding weights represent the weight of the body without other clothing.

April 16. Hemorrhage reduced considerably. Morning temperature, $98\frac{4}{5}$ ° F.; evening temperature, $98\frac{3}{5}$ ° F. Feels stronger.

April 17. Was propped up in bed. Is much improved. Stomach more retentive.

April 20. Weight 97 pounds. Scarcely any bleeding. Hydrastinine continued. Morning temperature, 99° F.; evening temperature, 98° F. Injected 17 minimis.

April 24. Sitting up in chair. Is very much improved.

April 27. Weight 98 pounds. Injected 20 minims. Able to walk about the room.

May 4. Walked down-stairs. Weight 100 pounds. The merest trace of bleeding. Stomach retentive.

May 11. Back in bed with an attack of tonsillitis, which lasted a week, temperature reaching 102° F. Weight 98½ pounds. Now injecting 20 minims every second day.

May 18. Stopped injections for one week. Vomiting returned. The temperature remains about 99° F. Weight 100 pounds.

May 25. Weight 102 pounds. Injecting 20 minims every third day. Temperature remains about 99° F. Vomiting is less frequent. Hemorrhage ceased entirely.

June 4. Weight 107 pounds. Injections stopped.

The injections were continued exactly two months. Their influence on the temperature was not marked either way. A careful record of her temperature, which was kept from April 4 to November 18, shows that, while at times it would be subnormal for a week, it never reached lower than 97° F., it was more frequently above normal, registering between 99° and 100° F. The only marked elevation of temperature she had was during the attack of tonsillitis. The influence of the injections on the weight is, however, more marked. It will be noticed that in the beginning of her trouble she weighed 186 pounds. The menorrhagia helped to reduce her to eighty-nine pounds. After the bleeding had ceased, and the injections increased to twenty minims per day, and the stomach became more retentive, she averaged one pound a week increase in weight. When the injections were stopped, the weight dropped seven pounds during the following four weeks, and remained stationary at 100 pounds for the succeeding month. Since that time—July—she has been steadily and progressively improving until she now (November 16, 1894) weighs 108 pounds. Her condition to-day is apparently that of a well woman, excepting that she still vomits her meals regularly. She has a good appetite. The bowels are regular. She is troubled occasionally with eructations of gas. She is in good spirits, the old spells of depression being entirely absent; the fainting attacks, frequent before, have now disappeared. She is able to do housework, to walk at her pleasure, and only extra exertion fatigues her. The duration of this case now extends over thirty months. While the objective symptoms remain about the same, the marked improvement in the subjective symptoms leads me to think the treatment has been of avail.

Remarks by Professor H. C. Wood.—So far as my reading and knowledge go there are no pathognomonic symptoms in Addison's disease, if

indeed, the so-called Addison's disease be not really a group of diseases ; but when I first saw the present case, the profound asthenia, the extraordinarily persistent and always seemingly causeless vomiting, and the distinct, though moderate, bronzing, in association with the apparently hopelessly progressive course of the disease, made a picture as typically resembling that of Addison's disease as can well be imagined. I do not, therefore, see how the diagnosis of Addison's disease can be gotten away from, unless the position be assumed that a certain case is not Addison's disease simply because it does not die ; and even if Professor Osler does say "the disease is in every case fatal," it hardly seems to me logical to deny a diagnosis on such grounds. Further, it is entirely clear that Mrs. E. is not yet well, although she is going about freely, and recently came without apparent fatigue from her country home to my office. At this visit the blood examination showed 75 per cent. hemoglobin, red corpuscles 4,800,000.

Moreover, the causeless vomiting still continues, a portion of almost every meal being thrown up ; and her weight has not yet nearly reached its former point. It should be remembered that in such a case, as in myxedema, it is not logical to suppose that the animal extract will cure. The theory of the application of the animal extracts is that so called "ductless glands," such as the thyroid body, the suprarenal capsules, and probably, also, the spleen, supply something that is necessary for the general nutrition, and that when a "ductless gland" is diseased, it is possible to imperfectly supply this needed material by material obtained from animals. Supplying the general nutritive need does not cure the diseased organ, though it gives temporary relief to the system ; and it is therefore evident that the artificial supply must be kept up indefinitely. I do not want to claim too much, but the results so far achieved in the present case are exceedingly interesting, and certainly make further trial of the remedy in other cases imperative.

PART II.

Graves's Disease. CASE I.—Spontaneous Cure Occurring During Abscess of the Spleen. CASE II.—Very Great Relief Apparently from the Use of Extract of Spleen.

By H. C. WOOD, M.D.

CASE I.—Miss H. J. first consulted me in the fall of 1893, giving the following history : In the spring of 1891, after a severe mental and physical strain caused by the long illness and death of a sister from exophthalmic goitre, she began to feel nervous and out of sorts, and to notice a lump growing in the lower part of her throat. Nevertheless, there was no marked failure of health until March, 1891, when, after seeing her father thrown from a carriage, she had an attack of chorea,

followed by increase in the size of the lump in the throat. She then went to Europe, and partially recovered her health, remaining, however, very nervous. March, 1893, after nursing an aunt through a long illness, there was great increase of the nervousness, which was now accompanied with persistent, severe palpitation of the heart. She went to Clifton Sanitarium, but grew worse under a course of baths, etc., losing twenty pounds ; and after coming home, in April, was one month in bed with great weakness, nervousness, frequent and severe palpitations of the heart, and distinct increase in the size of the lump. During the summer she very slowly improved under constant medical care, including climatic change, etc. November 29, 1893, she was sent to me by her physician, Dr. G. D. Nutt, of Williamsport.

The diagnosis was perfectly clear in that she had the peculiar nervous restlessness and irritability of old exophthalmic goitre, pronounced rapidity of the pulse, without cardiac murmur or any evidence of disease of the heart walls, and very pronounced enlargement of the thyroid gland. Careful examination of the eyes showed astigmatism, but no exophthalmia or other ocular lesions. She was treated with rest in bed, use of tonics, cardiants, and other remedies commonly employed in her disease. For a number of weeks careful trial was made of the application, twenty minutes twice a day, of Leiter's tubes, with very cold water, over the cardiac region. As the result of very numerous trials it was found that almost invariably a slight reduction of the pulse-rate followed the use of the tubes ; the average amount of reduction being three beats per minute. The average pulse taken daily before getting up in the morning was 95. She remained under care until Christmas, 1893, gaining somewhat in weight, and improving in her nervous condition, but without marked alteration either in the pulse or in the thyroid gland.

In January, 1894, Leiter's tubes were applied daily for twenty minutes to the thyroid gland, without any perceptible effect, unless it were a very slight increase in the pulse-rate immediately following the application. This increase was not sufficiently constant or great enough to be of any import. Under treatment she continued to very slowly improve. March 24, she was ordered five grains of the extract of thyroid gland to be taken by the mouth, three times a day, and two days later was sent to Virginia Beach. The extract of the gland was taken regularly until the early part of April, when she developed a violent exacerbation of her disease, attended with intense nervousness, much mental excitement, great sleeplessness, complete anorexia, and severe tachycardia. Although she herself believed that this exacerbation was due to the free use of atropia in her eyes under the orders of the oculist, the attack really began before her visit to the oculist ; and

unless it was produced by the thyroid extract was without apparent cause.

The night of April 26, Miss J. had slight pain in the left side of the abdomen, but was able to come the next morning to my office ; on returning, however, she was forced to go to bed by great increase of the pain. In the late evening there was a violent chill, followed by a rapid rise of temperature to 103° F. This was the commencement of a long illness, which was at first supposed to be a typhoid fever. The symptoms were continuous pain, with paroxysms of violent exacerbation in the splenic region, nausea, headache, mental distress, and anxiety; with a pulse which varied from 130 to 132, was always feeble and at times intermittent. There was at first some diarrhea (not dysenteric), which was followed by a tendency to constipation. The temperature had an almost regular range of from $99\frac{1}{2}^{\circ}$ in the morning to 103° F. in the evening ; some days, however, falling as low as 99° in the morning and ranging as high as 104° F. in the evening. Splenic enlargement became manifest on the second or third day, and rapidly increased ; the tumor being always intensely tender. The pain, which was very severe in the first few days of the illness, greatly abated at the end of the first week, but it never entirely disappeared, and returned with great severity in the fifth week.

The treatment was supporting and symptomatic. In the early part of the second week it was noted that the thyroid gland was becoming smaller, and by the fifth week it had entirely disappeared. In spite of all that could be done the patient developed under the long continuing fever the ordinary symptoms of a typhoid state to a very marked degree, presenting the aspect, indeed, of an advanced typhoid fever. The diagnosis of splenic abscess having been made, Professor J. William White was called in and agreed in the diagnosis. After careful discussion, however, it was decided to wait longer before operating, in order to allow close attachment to be formed between the spleen, and the abdominal walls. In the first week of June the temperature ranged between 101° and $101\frac{4}{5}^{\circ}$ in the morning and 103° and 104° F. in the evening. The general exhaustion was becoming alarming and the local splenic pain and tenderness more and more severe. June 6, Dr. White ran the needle of an aspirator into the centre of the spleen, and, obtaining seven or eight ounces of foul pus, cut into the seat of the abscess and inserted a drainage-tube. The shock from the operation was not very severe, but during the next eleven days the temperature ranged between 103° and 104° F. During this time the wound was regularly syringed out with antiseptics, and once or twice was re-opened and thoroughly explored without the finding of more pus. On the eleventh day after the operation the wound was still dis-

charging, but the temperature dropped to $99\frac{1}{2}$ ° F. in the morning, with an evening temperature of $102\frac{1}{2}$ ° F. There was, however, at this time profound exhaustion, with a very feeble pulse, 110 to 120; typhoid delirium at night and extreme mental feebleness in the day, with marked incoherency.

As the weather in Philadelphia was becoming very hot, on June 17 Miss J. was, by my advice, taken to Williamsport. She was moved in a basket stretcher, bore the journey fairly well; but was during it and afterwards incoherent not only in her speech but evidently in her mental action; being at times, indeed, delirious. This mental condition began to improve in about two weeks, but it was not until the latter part of July that she was able to find the right word to express her thoughts. The temperature a few days after her removal home fell, ranging for several weeks from 98° in the morning to 100° F. in the evening; the pulse ranged from 104 to 120. There was at first much nausea, occasional vomiting, and great loss of digestive power. She gradually improved, except for a few days, during the latter part of July, when she had an attack of severe acute indigestion and diarrhea, which reduced her greatly. August 16, convalescence seemed fairly established; the 1st of September she weighed ninety-one pounds, the 17th of September she weighed ninety-five pounds. By the latter date the wounds had healed completely; she was able to walk a little by herself, and digestion was good. The tongue was clean, the temperature normal, the bowels natural. The pulse was still quick, 115 to 120 beats per minute.

For an account of the case as embodied in the last paragraph, I am indebted to the nurse, who left the patient as convalescent in the last of September. In November I had the pleasure of a visit from her family physician, Dr. Nutt, who stated that Miss J., though not thoroughly strong, was very much better than she had been for years; that the pulse was about normal in rate; and that there had been no re-enlargement of the thyroid gland.

Remarks.—The clinical history of myxedema, as produced by removal of the thyroid body, indicates very strongly that there is some mysterious relation between that body and the spleen; removal of the thyroid being followed as a regular sequence by splenic enlargement. The extraordinary case just recorded certainly lends further credence to the theory of such relation, since there appears to have been a spontaneous cure of Graves's disease as the result of an acute splenitis ending in abscess. The cause of the splenitis remains obscure; it was finally attributed by the patient and I believe by Professor White to a wrench or injury received while dancing at the sea-shore; but, during the first four weeks of the disease, careful inquiry by myself failed entirely to

elicit from the patient any such incident, and at the end I was very doubtful as to the correctness of the theory.

From this and other cases which I have seen I am very strongly of the opinion that the exhibition of thyroid extract in Graves's disease usually is not negative in its result, but produces distinct exaggeration of the symptoms ; a fact which is in accord with that theory of Graves's disease which considers it to be a structural and functional hypertrophy of the thyroid body, a theory which finds further corroboration in the results which have been achieved in various cases by partial removal of the enlarged thyroid. If there be naturally a balance of function between the spleen and the thyroid body, and disturbance of one produces disturbance of the other ; and if extract of thyroid in myxedema with enlargement of the spleen does good whilst it does harm in Graves's disease, it is but a natural suggestion that the extract of spleen should be tried in cases of Basedow's disease. I have, therefore, had prepared a glycerin extract of beef spleen, but so far have had opportunity of using it only in one case, as follows :

CASE II.—Miss B., aged 24, dated beginning of her present illness to January, 1893, though it probably really began long before that time. February, 1894, entered the Orthopedic Hospital ; treated for ten weeks with rest cure with marked improvement, followed, however, by rapid return of the symptoms. Had menstruated but once in a year. On entering the University Hospital, October 14, 1894, there was marked exophthalmus, Von Graefe's symptom, however, being absent. Pulse, when quiet in bed, 92 to 98 ; temperature daily varying from one and a half to two degrees, usually subnormal in the morning. Patient extremely nervous. Thyroid much enlarged. Weight ninety-seven. She was put to bed for the greater part of the day, given massage, careful feeding, and 1-200 of atropine, three times a day, hypodermically. This treatment was kept up for eighteen days, with distinct improvement : weight then 101½ pounds, nervousness distinctly less, daily swing of the temperature reduced to about one degree. She was then put upon hypodermic injections of five minims of the splenic extract daily ; in a day or two this was increased to ten minims. No local irritation was produced by the injection. During the month of November she steadily improved, a marked reduction taking place in the size of the thyroid gland, her nervous symptoms disappearing, the pulse decreasing rapidly until it ranged between 82 and 90, and the bodily weight increasing seven pounds. In the fifth week after the institution of the treatment, menstruation, which had occurred only once in the previous twelve months, came on with great nervous disturbance, violent headache, abdominal pain, marked hysteria, etc. After menstruation the gain of the patient went on even more rapidly, and she was dis-

charged from the hospital early in the eighth week of treatment ; the thyroid gland was greatly diminished but had not quite disappeared ; the bodily weight had risen to $113\frac{1}{2}$ pounds, a gain of nearly two pounds a week after the institution of the treatment with the extract ; the pulse had become normal in rate, ranging from 74 to 82 ; the temperature had a regular daily swing of two-fifths of a degree only. She considered herself well, and one week later reported by letter that she was in excellent condition, in spite of the fact that she was actively visiting.

